the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.

58. A tandem fluorescent protein construct, comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and

wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Tyr66His and Tyr145Phe, or

b) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Ans212Lys, and

the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Cys or

b) Ser65Thr.

59. The construct of claim 57 or 58, wherein the linker moiety comprises between 5 amino acids and 50 amino acids.

60. The construct of claim 57 or 58, wherein the donor moiety acceptor moiety and the linker moiety are fused in a single amino acid sequence.

61. The construct of claim 57 or 58, wherein the linker comprises a cleavage recognition site for trypsin, enterokinase, HIV-1 protease, prohormone convertase, interleukin-1b-converting enzyme, adenovirus endopeptidase, cytomegalovirus assemblin, leishmanolysin, b-Secretase for APP, thrombin, renin, angiotensin-converting enzyme, cathepsin D or a kininogenase.

62. A recombinant nucleic acid coding for expression of a tandem fluorescent protein construct, the construct, comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties,

and wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or
b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or
c) Tyr66His and Tyr145Phe, or
d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or
e) Ser72Ala, Tyr145Phe and Thr203Ile, or
f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr, and

the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or
b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.

63. A recombinant nucleic acid coding for expression of a tandem fluorescent protein construct, the construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and

wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Tyr66His and Tyr145Phe, or

b) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Ans212Lys, and

the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Cys or

b) Ser65Thr.

64. The nucleic acid of claim 62 or 63, wherein the linker moiety comprises between 5 amino acids and 50 amino acids.

65. A host cell transfected with an expression vector comprising an expression control sequence operatively linked to a sequence coding for the expression of a tandem fluorescent protein construct, the construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and

wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or
b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or
c) Tyr66His and Tyr145Phe, or
d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or
e) Ser72Ala, Tyr145Phe and Thr203Ile, or
f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr, and

the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or
b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.

66. A host cell transfected with an expression vector comprising an expression control sequence operatively linked to a sequence coding for the expression of a tandem fluorescent protein construct, the construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and

wherein the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Tyr66His and Tyr145Phe, or
b) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Ans212Lys, and

the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Cys or

b) Ser65Thr.

67. The host cell of claim 65 or 66, further comprising a protease that is not naturally expressed by the host cell.

68. The host cell of claim 65 or 66, wherein the host cell is *E. coli.*

69. The host cell of claim 65 or 66, wherein the host cell is an eukaryotic cell.

70. The host cell of claim 65 or 66, wherein the host cell is a mammalian cell.

71. A method for measuring protease activity in a sample, comprising:

1) contacting the sample with the tandem fluorescent protein construct of claim 57 or 58 that comprises a linker moiety comprising a cleavage recognition site specific for the protease;

2) exciting the donor moiety by radiation; and

3) measuring fluorescence resonance energy transfer between the donor and acceptor moieties at a first time and a second time after addition of the tandem fluorescent protein construct whereby a decrease in fluorescence resonance energy transfer upon incubation of the sample with the tandem fluorescent protein construct indicates protease activity.

72. A method of measuring protease activity in a cell, comprising the steps of:

1) providing a cell that expresses the tandem fluorescent protein construct, of claim 57 or 58 that comprises a linker moiety comprising a cleavage recognition site specific for the protease;

2) exciting the donor moiety by radiation; and

3) measuring the degree of fluorescence resonance energy transfer between the donor and acceptor moieties wherein cleavage of the construct by the protease results in less fluorescence resonance energy transfer which reflects protease activity.

73. The method of claim 72, wherein the step of providing a cell comprises; inducing a sudden increase in expression of the tandem fluorescent protein construct, and the step of measuring the degree of fluorescence resonance energy transfer comprises; determining the degree at a first and a second time after induction of tandem fluorescent protein construct expression and determining the difference between the first and second time, whereby less fluorescence resonance energy transfer reflects the presence of the protease.

74. A method for determining whether a compound alters the activity of a protease comprising the steps of:

contacting a sample containing a known amount of the protease with the compound and with the tandem fluorescent protein construct of claim 57 or 58;

exciting the donor moiety by radiation; and

determining the degree of fluorescence resonance energy transfer between the donor and acceptor moieties in the sample containing the compound, and comparing the degree of fluorescence resonance energy transfer between the donor and acceptor moieties in a sample not containing the compound, whereby a difference in the degree of fluorescence resonance energy transfer indicates that the compound alters the activity of the protease.

75. A method for determining whether a compound alters the activity of a protease in a cell, comprising the steps of:

1) providing first and second cells that express the tandem fluorescent protein construct of claims 57 or 58, wherein the linker moiety comprises a cleavage recognition amino acid sequence specific for the protease;

2) contacting the first cell with an amount of the compound;

3) contacting the second cell with a different amount of the compound, or a buffer control;

4) exciting the donor moiety in the first and second cell by radiation;

5) determining the degree of fluorescence resonance energy transfer in the first and second cells; and

6) comparing the degree of fluorescence resonance energy transfer in the first and second cells, whereby a difference in the degree of fluorescence resonance energy transfer indicates that the compound alters the activity of the protease.

76. A tandem fluorescent protein construct, comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and wherein the donor or acceptor moieties comprises either,

an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising a mutation that reduces the hydrophobicity at positions A206, L221 or F223 and attenuates the intermolecular interactions between the donor or acceptor moieties,

or the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or

b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

c) Tyr66His and Tyr145Phe, or

d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or

e) Ser72Ala, Tyr145Phe and Thr203Ile, or

f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr,

or the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.

77. A recombinant nucleic acid coding for expression of a tandem fluorescent protein construct, the construct comprising construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and wherein the donor or acceptor moieties comprises either,

an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising a mutation that reduces the hydrophobicity at positions A206, L221 or F223 and attenuates the intermolecular interactions between the donor or acceptor moieties,

or the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or

b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

c) Tyr66His and Tyr145Phe, or

d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or

e) Ser72Ala, Tyr145Phe and Thr203Ile, or

f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr,

or the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.

78. A host cell transfected with an expression vector comprising an expression control sequence operatively linked to a sequence coding for the expression of a tandem fluorescent protein construct, the construct comprising construct comprising a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties and wherein the donor and acceptor moieties exhibit fluorescence resonance energy transfer ("FRET") when the donor moiety is excited by radiation, characterized in that the linker moiety comprises a protease cleavage recognition site, wherein cleavage of the linker by a protease results in a change in FRET between the donor and acceptor moieties, and wherein the donor or acceptor moieties comprises either,

an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising a mutation that reduces the hydrophobicity at positions A206, L221 or F223 and attenuates the intermolecular interactions between the donor or acceptor moieties,

or the donor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Phe64Leu, Ser65Thr, Tyr66Trp, Asn146Ile, Met153Thr, Val163A and Asn212Lys, or

b) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

c) Tyr66His and Tyr145Phe, or

d) Tyr66Trp, Asn146Ile, Met153Thr, Val163Ala and Asn212Lys, or

e) Ser72Ala, Tyr145Phe and Thr203Ile, or

f) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr,

or the acceptor moiety comprises an *Aequorea* fluorescent protein (SEQ. ID. No. 2) comprising the amino acid substitutions,

a) Ser65Gly, Val68Leu, Ser72Ala and Thr203Tyr, or

b) Ser65Thr, Ser72Ala, Asn149Lys, Met153Thr and Ile167Thr.--